

## WHAT IS CLAIMED IS:

1. A method of inhibiting hematopoiesis in a subject comprising downregulating an expression or activity of caspase-8 in the subject thereby inhibiting hematopoiesis therein.

2. The method of claim 1, wherein said downregulating said expression or activity of caspase-8 is effected by:

- (a) a molecule which binds caspase-8;
- (b) an enzyme which cleaves caspase-8;
- (c) an antisense polynucleotide capable of specifically hybridizing with an mRNA transcript encoding caspase-8;
- (d) a ribozyme which specifically cleaves transcripts encoding caspase-8;
- (e) a small interfering RNA (siRNA) molecule which specifically cleaves caspase-8 transcripts;
- (f) a non-functional analogue of at least a catalytic or binding portion of caspase-8
- (g) a molecule which prevents caspase-8 activation or substrate binding.
- (h) a vector for inducing and/or enhancing the endogenous production of an endogenous inhibitor of caspase-8; and/or
- (i) a vector for inhibiting the endogenous production of endogenous caspase-8.

3. The method of claim 2, wherein a sequence of said antisense polynucleotide is set forth by SEQ ID NO: 16.

4. The method of claim 2, wherein said molecule which binds caspase-8 is an antibody or antibody fragment.

5. The method of claim 4, wherein said antibody fragment is a Fab or a ScFv fragment.

6. The method of claim 2, wherein said molecule which binds caspase-8 is a caspase-8 inhibitor selected from the group consisting of z-VAD-fmk, IEDT-fmk and DEVD-fmk.

7. The method of claim 2, wherein a sequence of said small interfering RNA (siRNA) molecule is set forth by SEQ ID NO:15.

8. A method of inhibiting hematopoiesis in a subject, comprising downregulating an expression or activity of at least one polypeptide participating in the caspase-8 signaling pathway in the subject, thereby inhibiting hematopoiesis therein.

9. The method of claim 8, wherein said at least one polypeptide is selected from the group consisting of CASP3, CASP4, CASP6, CASP7, CASP9 and CASP10.

10. A method of treating a disorder characterized by hyperproliferation of hematopoietic cells, comprising downregulating an expression or activity of caspase-8 in the hematopoietic cells of a subject having the disorder, thereby treating said disorder characterized by hyperproliferation of said hematopoietic cells.

11. The method of claim 10, wherein said disorder is selected from the group consisting of acute myelogenous leukemia, acute myeloblastic leukemia, acute lymphocytic leukemia, acute prolymphocytic leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, chronic myeloid leukemia and myelodysplastic leukemia.

12. The method of claim 10, wherein said downregulating said expression or activity of caspase-8 is effected by:

- (a) a molecule which binds caspase-8;
- (b) an enzyme which cleaves caspase-8;
- (c) an antisense polynucleotide capable of specifically hybridizing with an mRNA transcript encoding caspase-8;

- (d) a ribozyme which specifically cleaves transcripts encoding caspase-8;
- (e) a small interfering RNA (siRNA) molecule which specifically cleaves caspase-8 transcripts;
- (f) a non-functional analogue of at least a catalytic or binding portion of caspase-8;
- (g) a molecule which prevents caspase-8 activation or substrate binding.
- (h) a vector for inducing and/or enhancing the endogenous production of an endogenous inhibitor of caspase-8; and/or
- (i) a vector for inhibiting the endogenous production of endogenous caspase-8.

13. The method of claim 12, wherein a sequence of said antisense polynucleotide is set forth by SEQ ID NO: 16.

14. The method of claim 12, wherein said molecule which binds caspase-8 is an antibody or antibody fragment.

15. The method of claim 14, wherein said antibody fragment is a Fab or a ScFv fragment.

16. The method of claim 12, wherein said molecule which binds caspase-8 is a caspase-8 inhibitor selected from the group consisting of z-VAD-fmk, IEDT-fmk and DEVD-fmk.

17. The method of claim 12, wherein a sequence of said small interfering RNA (siRNA) molecule is set forth by SEQ ID NO:15.

18. The method of claim 10, further comprising a chemotherapy.

19. The method of claim 10, further comprising a radiotherapy.

20. The method of claim 10, further comprising exposing said hematopoietic cells to one or more growth stimulating factors.

21. The method of claim 10, further comprising bone marrow transplantation.

22. The method of claim 21, wherein said bone marrow transplantation is autologous.

23. The method of claim 21, wherein said bone marrow transplantation is allogeneic.

24. A method of generating an hematopoietic cell population suitable for bone marrow replacement therapy, comprising:

- (a) isolating hematopoietic cells from a subject; and
- (b) exposing said hematopoietic cells to a molecule capable of downregulating an expression or activity of caspase-8 in said hematopoietic cells, thereby generating an hematopoietic cell population suitable for the bone marrow replacement therapy.

25. The method of claim 24, wherein said downregulating said expression or activity of caspase-8 is effected by:

- (a) a molecule which binds caspase-8;
- (b) an enzyme which cleaves caspase-8;
- (c) an antisense polynucleotide capable of specifically hybridizing with an mRNA transcript encoding caspase-8;
- (d) a ribozyme which specifically cleaves transcripts encoding caspase-8;
- (e) a small interfering RNA (siRNA) molecule which specifically cleaves caspase-8 transcripts;
- (f) a non-functional analogue of at least a catalytic or binding portion of caspase-8;
- (g) a molecule which prevents caspase-8 activation or substrate binding;
- (h) a vector for inducing and/or enhancing the endogenous production of an endogenous inhibitor of caspase-8; and/or

- (i) a vector for inhibiting the endogenous production of endogenous caspase-8.

26. The method of claim 25, wherein a sequence of said antisense polynucleotide is set forth by SEQ ID NO: 16.

27. The method of claim 25, wherein said molecule which binds caspase-8 is an antibody or an antibody fragment.

28. The method of claim 27, wherein said antibody fragment is a Fab or a ScFv fragment.

29. The method of claim 25, wherein said molecule which binds caspase-8 is a caspase-8 inhibitor selected from the group consisting of z-VAD-fmk, IEDT-fmk and DEVD-fmk.

30. The method of claim 25, wherein a sequence of said small interfering RNA (siRNA) molecule is set forth by SEQ ID NO:15.

31. A method of treating a disorder characterized by hyperproliferation of hematopoietic cells, comprising:

- (a) isolating the hematopoietic cells from a donor;
- (b) exposing said hematopoietic cells to a molecule capable of downregulating an expression or activity of caspase-8 in said hematopoietic cells; and
- (c) transplanting said hematopoietic cells into a recipient, thereby treating a disorder characterized by hyperproliferation of hematopoietic cells.

32. The method of claim 31, wherein said downregulating said expression or activity of caspase-8 is effected by:

- (a) a molecule which binds caspase-8;

- (b) an enzyme which cleaves caspase-8;
- (c) an antisense polynucleotide capable of specifically hybridizing with an mRNA transcript encoding caspase-8;
- (d) a ribozyme which specifically cleaves transcripts encoding caspase-8;
- (e) a small interfering RNA (siRNA) molecule which specifically cleaves caspase-8 transcripts;
- (f) a non-functional analogue of at least a catalytic or binding portion of caspase-8;
- (g) a molecule which prevents caspase-8 activation or substrate binding.
- (h) a vector for inducing and/or enhancing the endogenous production of an endogenous inhibitor of caspase-8; and/or
- (i) a vector for inhibiting the endogenous production of endogenous caspase-8.

33. The method of claim 32, wherein a sequence of said antisense polynucleotide is set forth by SEQ ID NO: 16.

34. The method of claim 32, wherein said molecule which binds caspase-8 is an antibody or an antibody fragment.

35. The method of claim 34, wherein said antibody fragment is a Fab or a ScFv fragment.

36. The method of claim 32, wherein said molecule which binds caspase-8 is a caspase-8 inhibitor selected from the group consisting of z-VAD-fmk, IEDT-fmk and DEVD-fmk.

37. The method of claim 32, wherein a sequence of said small interfering RNA (siRNA) molecule is set forth by SEQ ID NO:15.

38. The method of claim 31, wherein said donor is said recipient.

39. The method of claim 31, wherein said donor is allogeneic to said recipient.

40. The method of claim 31, wherein said disorder is selected from the group consisting of acute myelogenous leukemia, acute molympocytic leukemia, acute lymphocytic leukemia, acute prolymphocytic leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, chronic myeloid leukemia and moldering leukemia.

41. The method of claim 31, wherein step (b) further comprising exposing said hematopoietic cells to one or more growth stimulating factors.

42. An article-of-manufacture comprising packaging material and a pharmaceutical composition identified for use in modulating hematopoiesis being contained within the packaging material, said pharmaceutical composition including, as an active ingredient, an agent capable of modifying an activity or an expression of caspase-8 in a subject and a pharmaceutically acceptable carrier.

43. The article of manufacture of claim 42, wherein said agent is capable of at least partially inhibiting said expression or activity of said caspase-8.

44. The article of manufacture of claim 43, wherein said agent is selected from the group consisting of:

- (a) a molecule which binds caspase-8;
- (b) an enzyme which cleaves caspase-8;
- (c) an antisense polynucleotide capable of specifically hybridizing with an mRNA transcript encoding caspase-8;
- (d) a ribozyme which specifically cleaves transcripts encoding caspase-8;
- (e) a small interfering RNA (siRNA) molecule which specifically cleaves caspase-8 transcripts;
- (f) a non-functional analogue of at least a catalytic or binding portion of caspase-8;
- (g) a molecule which prevents caspase-8 activation or substrate binding;

- (h) a vector for inducing and/or enhancing the endogenous production of an endogenous inhibitor of caspase-8; and/or
- (i) a vector for inhibiting the endogenous production of endogenous caspase-8.

45. The use of a downregulator of an expression or activity caspase-8 in the manufacture of a medicament for the inhibition of hematopoiesis.

46. The use of a downregulator of an expression or activity caspase-8 for treating a disorder characterized by hyperproliferation of hematopoietic cells.

47. The use according to claim 46, wherein said disorder is selected from the group consisting of acute myelogenous leukemia, acute molympocytic leukemia, acute lymphocytic leukemia, acute prolymphocytic leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, chronic myeloid leukemia and moldering leukemia.

48. The use according to claims 45 or 46, wherein said downregulating said expression or activity of caspase-8 is effected by:

- (a) a molecule which binds caspase-8;
- (b) an enzyme which cleaves caspase-8;
- (c) an antisense polynucleotide capable of specifically hybridizing with an mRNA transcript encoding caspase-8;
- (d) a ribozyme which specifically cleaves transcripts encoding caspase-8;
- (e) a small interfering RNA (siRNA) molecule which specifically cleaves caspase-8 transcripts;
- (f) a non-functional analogue of at least a catalytic or binding portion of caspase-8;
- (g) a molecule which prevents caspase-8 activation or substrate binding.
- (h) a vector for inducing and/or enhancing the endogenous production of an endogenous inhibitor of caspase-8; and/or
- (i) a vector for inhibiting the endogenous production of endogenous caspase-8.

49. The use of claim 48, wherein a sequence of said antisense polynucleotide is set forth by SEQ ID NO: 16.



50. The use of claim 48, wherein said molecule which binds caspase-8 is an antibody or antibody fragment.

51. The use of claim 50, wherein said antibody fragment is a Fab or a ScFv fragment.

52. The use of claim 48, wherein said molecule which binds caspase-8 is a caspase-8 inhibitor selected from the group consisting of z-VAD-fmk, IEDT-fmk and DEVD-fmk.

53. The use of claim 48, wherein a sequence of said small interfering RNA (siRNA) molecule is set forth by SEQ ID NO:15.

54. The use of claims 45 or 46, further comprising a chemotherapy.

55. The use of claims 45 or 46, further comprising a radiotherapy.

56. The use of claims 45 or 46, further comprising exposing said hematopoietic cells to one or more growth stimulating factors.

57. The use of claims 45 or 46, further comprising bone marrow transplantation.

58. The use of claim 57, wherein said bone marrow transplantation is autologous.

59. The use of claim 57, wherein said bone marrow transplantation is allogeneic.

60. The use of a downregulator of at least one polypeptide participating in the caspase-8 signaling in the manufacture of a medicament for the treatment of a disorder characterized by hyperproliferation of hematopoietic cells.

61. The use of claim 60, wherein said disorder is selected from the group consisting of acute myelogenous leukemia, acute molympocytic leukemia, acute lymphocytic leukemia, acute prolymphocytic leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, chronic myeloid leukemia and moldering leukemia.
62. The use of claim 60, wherein said at least one polypeptide is selected from the group consisting of CASP3, CASP4, CASP6, CASP7, CASP9 and CASP10.